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Review

Reaching women who do not participate in the regular cervical cancer screening programme by offering self-sampling kits: A systematic review and meta-analysis of randomised trials

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Abstract ***Introduction:*** Population coverage for cervical cancer screening is an important determinant explaining differences in the incidence of cervical cancer between countries. Offering devices for self-sampling has the potential to increase participation of hard-to-reach women.
Methods: A systematic review and meta-analysis were performed to evaluate the participation after an invitation including a self-sampling device (self-sampling arm) versus an invitation to have a sample taken by a health professional (control arm), sent to under-screened women.
Results: Sixteen randomised studies were found eligible. In an intention-to-treat analysis, the pooled participation in the self-sampling arm was 23.6% (95% confidence interval (CI) = 20.2–27.3%), when self-sampling kits were sent by mail to all women, versus 10.3% (95% CI = 6.2–15.2%) in the control arm (participation difference: 12.6% [95% CI = 9.3–15.9]). When women had to opt-in to receive the self-sampling device, as used in three studies, the pooled participation was not higher in the self-sampling compared to the control arm (participation difference: 0.2% [95% CI = −4.5–4.9%]).
Conclusion: An increased participation was observed in the self-sampling arm compared to the control arm, if self-sampling kits were sent directly to women at their home address. However, the size of the effect varied substantially among studies. Since participation was similar in both arms when women had to opt-in, future studies are warranted to discern opt-in scenarios that are most acceptable to women.

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1. Introduction

Well organised screening programmes have reduced the incidence and mortality of cervical cancer substantially in many industrialised countries [1–4]. However, screening coverage is not always optimal [5–10]. In the context of organised screening, women who are never screened or under-screened have an increased risk of invasive cervical cancer [11–13].

Several reasons have been identified as to why women do not attend cervical cancer screening. Barriers for participation in cytological screening do not only include practical (i.e. transport to the clinic, inconvenient clinic hours), economical and educational factors, but also personal-level factors, such as embarrassment and fear of pain [14].

With the introduction of testing for high-risk HPV (hrHPV) as a primary screening test in cervical cancer prevention [15–18], samples taken by the woman herself (self-samples) have gained broad attention due to its potential to increase screening attendance. Furthermore, it has been shown that the accuracy of hrHPV DNA testing on a self-sample is similar to that of a sample collected by a clinician, if validated PCR tests are used [19,20].

In most studies, the acceptability, preferences and attitudes of women towards self-sampling are positive, yet some negative findings have been published [21,22]. Data from a recent review [23] and a meta-analysis [24] indicate that, overall, offering self-sampling can be superior to a reminder invitation for cytology in attracting women who never or irregularly participated in the cervical cancer screening programme. However, heterogeneity among studies is considerable. Given that the participation rate is a fundamental factor determining the (cost-)effectiveness of self-sampling, careful consideration of elements that may influence its success is essential. In this study, an updated review and meta-analysis is performed, including studies published until 2015. The relative participation and participation difference of the self-sampling arm compared to the control arm are calculated in a per-protocol and intention-to-treat analysis. Furthermore, a systematic evaluation of the heterogeneity across studies is performed, by comparing the effect of different methods to invite women for self-sampling.

2. Materials & methods

This systematic review and meta-analysis evaluates whether offering a kit for self-sampling (at home) could increase screening attendance, compared to sending reminder letters for a Pap smear or HPV test on a sample collected by a clinician (at the clinic).

The literature search was performed using electronic bibliographic databases Medline (PubMed), EMBASE, and CENTRAL. A general search string was constructed and included substrings on four topics, combined by an AND-operator (1: cervical cancer, 2: HPV, 3: self-sampling, and 4: participation in screening) (Box S1, in supplementary online material). The search string was adjusted to the search syntax of each database. No language or publication date restrictions were applied. Additionally, a manual search for eligible studies was performed by browsing through the citation lists of relevant reports.

Studies with a randomised design were eligible if the following criteria were met: (1) the study population involved irregularly or never-screened women, or women who did not respond to $\geqslant 1$ invitation for conventional screening for cervical cancer, (2) women in the intervention-group (self-sampling arm) were invited to collect a self-sample for hrHPV testing (3) women in the control group (control arm) were invited to undergo conventional cytology screening and/or hrHPV testing on a sample taken by a clinician, (4) the participation in the self-sampling arm and the control arm was documented, and (5) a minimum of 1000 women were included in the study. A minimal study size of 1000 participants was implemented to allow sufficient precision for all outcomes (e.g. test-positivity, compliance to follow-up, and detection of cervical intraepithelial neoplasia grade two or worse (CIN2+)). Women whose last screening exceeded the locally defined screening interval were considered as irregularly screened women. In this review, the term under-screened will be used to refer to any of the categories described above (irregularly screened, never-screened, or non-responders to a screening invitation). Diverse methods of invitation were accepted (directly sending the self-sampling kit by mail, door-to-door approach, community counselling or opt-in invitations).

Data on the participation in the self-sampling arm and the control arm were extracted by FV and MA. Discordances between reviewers were resolved by discussion. If available, data on sample adequacy, test-positivity, compliance to follow-up among women with a positive screening test, and detection of CIN2+ were extracted for both arms. Information on the design of the study and on influential study characteristics (such as scenario of invitation, urban/rural area, invitation history, and age) was extracted to allow assessment of sources of heterogeneity. The quality of included studies was evaluated using the Cochrane Collaboration's tool for risk of bias in randomised trials [25]. Three topics were appraised in particular: selection bias, attrition bias and reporting bias. The performance and detection bias parameters in the tool, were considered not applicable since blinding is not possible due to the clearly different nature of the intervention (self-collected sampling at home versus cytology or clinician-collected sampling at the clinic).

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